Health Canada Santé Canada

Your health and safety... our priority. *Votre santé et votre sécurité... notre priorité.*

Registration Decision RD2010-06

Acetamiprid

(publié aussi en français)

16 September 2010

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6604-E2
Ottawa, Ontario
K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

Canada

HC Pub: 100347

ISBN: 978-1-100-16218-8 (978-1-100-16219-5)
Catalogue number: H113-25/2010-6E (H113-25/2010-6E-PDF)

© Her Majesty the Queen in Right of Canada, represented by the Minister of Health Canada, 2010

All rights reserved. No part of this information (publication or product) may be reproduced or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, or stored in a retrieval system, without prior written permission of the Minister of Public Works and Government Services Canada, Ottawa, Ontario K1A 0S5.

Table of Contents

Registration Decision for Acetamiprid 1

What Does Health Canada Consider When Making a Registration Decision? 1

Health Considerations 2

Environmental Considerations 5

Value Considerations 5

Measures to Minimize Risk 6

Other Information 8

List of Abbreviations 9

Appendix I Comments and Responses 11

Table 1 Mixer/loader dermal and inhalation exposure estimates for Assail 70WP Insecticide - Addendum to Table 6 of PRD2010-02 15

References 17

Registration Decision for Acetamiprid

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Acetamiprid Technical Insecticide, Assail 70 WP Insecticide, Tristar 70 WSP Insecticide, Acetamiprid RTU Insecticide, and Vault 50 FS Insecticide Seed Treatment containing the technical grade active ingredient acetamiprid to control a variety of insect pests in various fruit, vegetable, ornamental and oilseed crops.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2010-02, *Acetamiprid*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for acetamiprid and summarizes the Agency's decision, the reasons for it and provides, in Appendix I, a summary of comments received during the consultation process as well as the PMRA's response to these comments. This decision is consistent with the proposed registration decision stated in PRD2010-02.

For more details on the information presented in this Registration Decision, please refer to the related Proposed Registration Decision PRD2010-02, *Acetamiprid* that contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

---

1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act*" ...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What Is Acetamiprid?

Acetamiprid is a neonicotinoid insecticide that is active against insects on contact as well as through ingestion, and it is distributed systemically within plants. End-use products containing acetamiprid are registered for use on a variety of food crops and ornamentals by conventional ground application and for use as a seed treatment on canola and mustard seed.

Health Considerations

Can Approved Uses of Acetamiprid Affect Human Health?

Acetamiprid is unlikely to affect your health when used according to label directions.

Exposure to acetamiprid may occur through diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when using acetamiprid products according to label directions.

The technical grade active ingredient acetamiprid showed high acute toxicity to rats when ingested. Consequently, the statement "Danger Poison" is required on the label for the technical grade active ingredient. The end-use products Assail 70 WP Insecticide and Tristar 70 WSP Insecticide caused moderate acute toxicity in animals when ingested. Consequently, the statement "Warning Poison" is required on the labels for these end-use products.

Acetamiprid does not cause cancer in animals and does not damage genetic material such as DNA. Health effects in animals given daily doses of acetamiprid over long periods of time included generalized toxicity manifested as effects on body weight and food consumption, as well as mild, non-adverse effects on the liver as it adapted to an increased demand to metabolize acetamiprid.

Acetamiprid does not cause birth defects in animals. There was evidence in animals that the young are more sensitive to the effects of acetamiprid than adults. Effects on the young animal were considered more serious than those observed in parental animals at the same dose level. In addition, signs suggestive of neurotoxicity were observed in young animals at doses lower than those that caused effects in parental animals.

The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing infants). Only those uses where exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Residues in Water and Food

Dietary risks from food and water are not of concern

Aggregate dietary intake estimates (food plus water) revealed that children less than two years of age – the subpopulation which would ingest the most acetamiprid relative to body weight – are expected to be exposed to less than 8.4% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from acetamiprid is not of concern for all population sub-groups. A cancer potency factor (Q_1^*) has not been established for acetamiprid. Therefore, a cancer dietary risk assessment is not required.

An aggregate (food plus water) dietary intake estimate for the highest exposed population (children one to two years old) used less than 95% of the acute reference dose, which is below the level of concern. Therefore, the acute dietary risk from acetamiprid is below the level of concern for all population sub-groups.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Confirmatory residue trials conducted throughout Canada using acetamiprid on leafy vegetables, cole crops, field tomatoes, pome fruit and grapes were acceptable. MRLs will not be revised as a result of this evaluation. As such, please refer to the MRL table for this active ingredient on the Health Canada website.

Risks in Residential and Other Non-Occupational Environments

All uses currently registered for the domestic ready-to-use product are not of concern, and entry by the public into treated commercial areas is considered acceptable.

Exposure of the general population to residues of acetamiprid from orchards treated with Assail 70 WP Insecticide could occur by participating in pick-your-own (U-pick) activities for apples and pears. The exposure from such activities were considered acceptable for adults, youths, and children.

Exposure could also occur from homeowners spraying Acetamiprid RTU Insecticide, and subsequently re-entering treated residential areas. Both the use and postapplication exposures to adults, youth and children were considered acceptable.

Occupational Risks From Handling Assail 70 WP Insecticide, Tristar 70 WSP Insecticide and Vault 50 FS Insecticide Seed Treatment

Occupational risks are not of concern when Assail 70 WP Insecticide, Tristar 70WSP Insecticide and Vault 50 FS Insecticide Seed Treatment are used according to the proposed label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply Assail 70 WP Insecticide, Tristar 70 WSP Insecticide and Vault 50 FS Insecticide Seed Treatment as well as field workers re-entering treated fields, nurseries, greenhouses, shadehouses and lathhouses can come in direct contact with acetamiprid residues on the skin, or by inhalation. Therefore, the labels specify that anyone mixing, loading and applying these products must wear: a long-sleeved-shirt, long pants, socks and shoes, and chemical-resistant gloves. In addition, depending on the product, workers may require chemical-resistant coveralls and/or a respirator. The labels also require that workers do not enter treated fields or other treated sites for at least 12 hours after application, or longer, depending on the tasks to be performed. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risks to these individuals are determined not to be of concern.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Acetamiprid Is Introduced Into the Environment?

Acetamiprid poses a potential risk to non-target organisms including terrestrial plants, marine-estuarine invertebrates (such as the mysid shrimp) and non-target pollinators (such as honeybees). Therefore, risk-reduction measures including precautionary label statements and buffer zones must be observed.

The environmental fate and environmental toxicology of acetamiprid is described in REG2002-05.

The environmental transformation products of acetamiprid, IM-1-5 in soil, IM-1-4 in sediment, and IB-1-1 in water are not expected to accumulate or move in the environment, nor pose a risk to non-target organisms.

Acetamiprid will pose negligible risk to earthworms under conditions of field use. The risk to avian reproduction is also negligible. It will, however, pose a risk to aquatic invertebrates, non-target terrestrial plants and honey bees exposed to direct treatment. These risks can be mitigated by precautionary label statements and the establishment of terrestrial and aquatic buffer zones for protection of these habitats.

Value Considerations

What is the Value of Assail 70 WP Insecticide, Tristar 70 WSP Insecticide, Acetamiprid RTU Insecticide, and Vault 50 FS Insecticide Seed Treatment?

Pest control products containing acetamiprid control a variety of insect pests in various fruit, vegetable, ornamental, and oilseed crops.

Assail 70 WP Insecticide is registered for commercial use to control aphids, whitefly, Colorado potato beetle, tentiform leafminer, leafhoppers, codling moth, pear psylla, swede midge, oriental fruit moth, and pea leafminer on leafy vegetables, cole crops, certain fruiting vegetables, pome fruits, grapes, potato, and tobacco.

Tristar 70 WSP Insecticide is registered for commercial use to control European pine sawfly, aphids, tentiform leafminer, leafhoppers, and whiteflies on ornamentals, including trees, potted flowering plants, foliage plants, bedding plants, and flowers grown for cuttings, outdoors and in greenhouses, lathhouses, and shadehouses.

Acetamiprid RTU Insecticide is registered for domestic use to control aphids, European pine sawfly, leafhoppers, whiteflies, tentiform leafminer, and Colorado potato beetle on flowers and ornamental plants, leafy vegetables, cole crops, field tomatoes, and pome fruits.

Vault 50 FS Insecticide Seed Treatment is registered for commercial use as a seed treatment to control flea beetles on canola and mustard.

Please see the registered product labels for complete details of the registered uses.

Acetamiprid is an alternative to other insecticides currently registered for use on the pests and crops previously listed. Alternatives such as acetamiprid are needed to help prevent the development of resistance to registered insecticides and to provide replacements for older insecticides that may become unavailable as a result of re-evaluation.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label of Acetamiprid Technical Insecticide, Assail 70 WP Insecticide, Tristar 70 WSP Insecticide, Acetamiprid RTU Insecticide, and Vault 50 FS Insecticide Seed Treatment to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

Human Health

There is a concern for users coming into direct contact with acetamiprid on the skin or through inhalation of spray mists. Therefore, anyone mixing, loading or applying Assail 70 WP Insecticide must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. In addition, when mixing or loading certain amounts of product for application to potatoes they must also wear chemical-resistant coveralls and a respirator.

When mixing, loading or applying Tristar 70 WSP Insecticide for outdoor use, handlers and applicators must wear a long-sleeved shirt, long pants, socks and shoes, and chemical-resistant gloves. When applying indoors, handlers and applicators must wear chemical-resistant coveralls over a long-sleeved shirt and long pants, chemical-resistant gloves, rubber boots, goggles or faceshield, and a respirator.

For all tasks relating to treating seed (including mixing, loading, or treating) using Vault 50 FS Insecticide Seed Treatment, workers must wear chemical-resistant coveralls over long-sleeved shirt and long pants, chemical-resistant gloves, socks and shoes, and a respirator. Planters of treated seed must wear coveralls over long-sleeved shirt, long pants, socks and shoes, and chemical-resistant gloves.

A 12-hour restricted-entry interval (REI) for the agricultural products encompasses most postapplication tasks, however, it is necessary for longer REIs for some tasks on several crops, including cole crops, pome fruits and grapes. Other mitigation measures include the reduction of application rate, increased time interval between sprays and restrictions on the amount of product that can be handled in a day. Exposure concerns could not be reconciled for aerial use on potato crops, therefore, this use can not be supported. Standard label statements to protect against drift during application are on the label.

All use statements on the currently registered label of Acetamiprid RTU Insecticide are acceptable.

Environment

Key risk-reduction measures for the protection of the environment include precautionary label directions and buffer zones. These measures were originally described in REG2002-05 and are summarized here for the current end-use products and the technical active ingredient.

Assail 70 WP Insecticide and Tristar 70 WSP Insecticide

- Toxicity statements for aquatic organisms, non-target terrestrial plants, and bees
- Restriction on use when bees are in the area
- Terrestrial buffer zones of 2 m and 10 m for field sprayer and airblast application, respectively
- Aquatic buffer zones of 20 m and 30 m for field sprayer and airblast application, respectively

Vault 50 FS Insecticide Seed Treatment

- Toxicity statements for aquatic organisms, non-target terrestrial plants, bees and birds
- Directions to remove any seeds left on soil surface

Acetamiprid RTU Insecticide

- Toxicity statements for aquatic organisms, non-target terrestrial plants, and bees
- Restriction of use when bees are in the area
- No application to bodies of water and no application during gusty winds

Acetampirid Technical

- Toxicity statement for aquatic organisms, non-target terrestrial plants, and bees
- Precaution statement for discharge of effluent into bodies of water

Other Information

The relevant test data on which the decision is based (as referenced in this document) are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

List of Abbreviations

µg	micrograms
a.i.	active ingredient
bw	Body weight
CFIA	Canadian Food Inspection Agency
DNT	developmental neurotoxicity
GAP	good agricultural practices
i.e.	that is
kg	kilogram
LD_{50}	lethal dose 50%
LOC	level of concern
mg	milligram
PCPA	*Pest Control Products Act*
PMRA	Pest Management Regulatory Agency
ppm	parts per million
US EPA	United States Environmental Protection Agency

Appendix I Comments and Responses

1. Comments on label mitigation for birds and bees.

A comment received on the document Proposed Registration Decision - *Acetamiprid* (PRD2010-02), indicated that toxicity statements on product labels addressing mitigation of potential exposure to bees and birds was unwarranted.

Response:

Bees

It should be noted that the requirement for toxicity statements on product labels is determined on a hazard (toxicity) basis and/or a risk basis. Due to the inherent toxicity of acetamiprid to bees, this product meets the hazard labelling criteria. Data from the original review (summarized in the REG2002-05) indicate that the acute contact LD_{50} of acetamiprid to the honeybee (*Apis mellifera*) is 8.09 µg a.i./bee. This categorizes acetamiprid as moderately toxic to bees (according to the standard classification system by Atkins *et al.*, 1981). A hazard-based statement (i.e. "toxic to bees") is required on the product label when the LD_{50} is less than 11 µg a.i./ bee. The statement regarding restriction of use when bees are in the area is required in order to reduce the potential for acetamiprid exposure. Thus, these statements must remain on the product labels.

Birds

As stated above, the requirement for toxicity statements on product labels are determined on a hazard (toxicity) basis and/or a risk basis. Due to the inherent toxicity of acetamiprid to birds, this product meets the hazard labelling criteria. Data from the original review (summarized in the REG2002-05) indicate that the acute (14 day) oral LD_{50} of acetamiprid to the mallard duck (*Anas platyrhynchos*) was 84 mg a.i./kg bw. This categorizes acetamiprid as moderately toxic to birds (according to the standard classification system by the US EPA). The following hazard-based statements: "Toxic to birds" and "Any spilled or exposed seeds must be incorporated into the soil or otherwise cleaned-up from the soil surface." must remain on the seed treatment product label (Vault 50 FS Insecticide Treatment – Registration number 28119).

For further details on the potential risk to honey bees and birds from exposure to acetamiprid are provided in REG2002-05.

2. Comments on the reference to nicotine.

A comment received on the document Proposed Registration Decision - *Acetamiprid* (PRD2010-02) questioned the suitability/appropriateness of comparing acetamiprid with nicotine.

Response:

Neonicotinoids are known to be similar to nicotine in their structure and action as agonists of the nicotinic acetylcholine receptor. While a full toxicological database is available for acetamiprid, there is an abundance of research available on nicotine, and the findings from this research cannot be ignored. It is agreed that exposure to acetamiprid is not analogous to exposure to cigarette smoke. In fact, most of the published studies cited

in PRD2010-02 involved direct dosing of nicotine itself, and not exposure to cigarette smoke. It is also recognized that, in general, mammalian receptors have lower affinity for neonicotinoids than insect receptors. On the other hand, nicotine is a more potent agonist in mammals than in insects. As such, the literature studies examining the effects of nicotine on the developing nervous system were used qualitatively in a weight of evidence assessment of the effects noted in the acetamiprid toxicological database.

3. Comments on safety factors.

A comment was received that the use of an additional 3-fold PCPA factor applied to infants and children, as reported in the document Proposed Registration Decision, *Acetamiprid* (PRD2010-02), was unwarranted.

Response:

The comments stated that "the toxicological endpoint selected is an endpoint that specifically addresses sensitivity of the young, prenatal, and postnatal toxicity". It is assumed that, with this statement, it is argued that the 3-fold PCPA factor is not required in the risk assessments for acetamiprid since the point of departure is based on the critical endpoint in the sensitive population.

As discussed in the PMRA's Science Policy Note (SPN 2008-01), the PMRA must apply a default 10-fold PCPA factor unless the PMRA concludes, based on reliable data, that a different factor is appropriate for the protection of infants and children. Determination of the magnitude of the factor involves evaluating the completeness of the data with respect to exposure of and toxicity to infants and children as well as the potential for prenatal or postnatal toxicity. In the case of acetamiprid, the database was considered complete and adequate to evaluate prenatal and postnatal toxicity. Thus, the determination of the magnitude of the PCPA factor in the risk assessment for acetamiprid was based primarily on concerns relating to prenatal and postnatal toxicity.

It is recognized that if the point of departure is based on the critical endpoint in the sensitive population, the PCPA factor could be obviated with respect to prenatal and postnatal toxicity. However, in addition to evidence for sensitivity of the young noted in the database, the seriousness of the prenatal or postnatal endpoints, among other factors, is considered in determining the level of concern for prenatal and postnatal toxicity. If the critical endpoint is based on a serious toxicological effect, a high degree of concern would be identified. One of the criteria for the establishment of a serious toxicological effect for a pesticide is persistent or significant disability or incapacity. The temporal nature of the effect (for example, time of onset, persistence, recovery, etc.) will influence the determination of the degree of concern, with irreversible findings eliciting greater concern. Concern for prenatal or postnatal toxicity is heightened if sufficient human data are available to judge that an adverse developmental effect is related to exposure. Such information could arise from the literature and include epidemiological information.

If the overall level of concern for prenatal and postnatal toxicity is high, the full 10-fold PCPA factor is retained. A different PCPA factor could be used based on the level of uncertainty regarding the potential for prenatal and postnatal toxicity.

Although the database for acetamiprid is considered to be complete with respect to the assessment of prenatal and postnatal toxicity, the results of the DNT study demonstrated increased sensitivity of the young. Auditory startle response was affected in neonatal rats at doses lower than those that resulted in toxicity to maternal animals. This effect persisted into adulthood, long after exposure to the test chemical had ceased. As discussed in PRD2010-02, there is also uncertainty with respect to the seriousness of this endpoint in humans. What was manifested as an effect on auditory startle in young rats may manifest in humans as a disabling or incapacitating condition, in other words, a serious endpoint. In the case of acetamiprid, the similarities between neonicotinoids and nicotine and the evidence suggesting that exposure to nicotine results in impaired neurological development in humans and rats were taken into consideration in determining the level of concern for prenatal and postnatal toxicity. The retention of a 3-fold PCPA factor was deemed necessary to protect infants and children from the potential effects acetamiprid could have on the developing nervous system, given the uncertainty regarding the seriousness of the endpoint in humans.

The comment also included the argument that the 3-fold PCPA factor is not required since any uncertainty with respect to how the endpoint would manifest in humans is accounted for by the interspecies uncertainty factor. The PMRA strives to ensure that "double counting" among the uncertainty factors does not occur. The 10-fold interspecies uncertainty factor addresses the uncertainty inherent in the extrapolation of information from experimental animal species to humans. It is considered to reflect inherent differences in toxicokinetics and toxicodynamics between species.

Extrapolating an endpoint such as liver toxicity from a laboratory animal to a human involves a level of uncertainty that is captured in the standard 10-fold uncertainty factor for interspecies extrapolation. In the case of acetamiprid, the concern regarding the manner in which the developmental neurotoxicity endpoint would manifest in a developing human stems from the nature of the testing paradigm. The DNT study is designed to be a screening tool to identify the potential for effects on the developing nervous system. As discussed in PRD2010-02, the available bioassays conducted with acetamiprid were not designed to test for more subtle neurotoxic effects such as attention deficit and mood disorders. It is not known how a response in the rat in a very simple test of cognitive ability, such as the test for auditory startle response, would translate to functional effects in a human. For example, studies in humans have demonstrated reduced acoustic startle response in patients with obsessive compulsive disorder (Hoenig et al., 2005) and schizophrenia (Takahashi et al., 2008). It is not known if the reduced auditory startle response observed in the rat is an indication of a more serious and more complex disorder that would develop in the human. In this particular case, the concern lies with the uncertainty regarding seriousness of the endpoint and thus the potential for prenatal and postnatal toxicity, which is captured under the PCPA factor. The evidence linking nicotine exposure in animals and exposure to cigarette smoke in humans to cognitive deficits add to this concern. Thus, it was considered appropriate to retain a 3-fold PCPA factor in the risk assessments for acetamiprid.

4. **Comments on potential refinement of the acute dietary exposure analysis.**
The PMRA was requested to reexamine the input parameters used in the acute dietary exposure analysis reported in the document Proposed Registration Decision, *Acetamiprid* (PRD2010-02).

Response:
At the present time, all available refinements (including CFIA monitoring data for apples) have been used for the acute dietary risk assessment. As additional monitoring data becomes available, the risk assessment may be further refined.

In the meantime, to further refine the risk assessment, the petitioner is encouraged to provide additional trials for collards and/or mustard greens conducted in Canadian growing regions according to the Canadian GAP. The current assessment includes a maximum residue of 1.1 ppm for mustard greens that was translated to collards. The trial was conducted in Texas, and the rate was 1.4-fold the approved Canadian GAP. Of the remaining eight trials, only one was conducted in a Canadian growing region (R5). The range in maximum residues in the eight remaining trials was 0.105–0.725 ppm.

Therefore, until additional monitoring data becomes available, the petitioner may wish to consider generating Canadian trial data that will enable the PMRA to further refine the acute dietary risk assessment.

5. **Comments on re-entry intervals.**
Clarification was requested for the Tristar label with respect to re-entry intervals for greenhouse and outdoor settings.

Response:
The restricted-entry interval (REI) of 12 hours after application applies to both greenhouse and outdoor uses, and is a standard postapplication re-entry statement on products. This statement assumes that workers entering the treated outdoor area or greenhouse will conduct postapplication tasks that may involve direct contact with treated foliage. Re-entry to a treated greenhouse to conduct activities not involving contact with the treated crop is permitted within the 12 hour REI.

The greenhouse foliar treatments use spray equipment that is not expected to require a specific ventilation program. The required restricted-entry interval (REI) of 12 hours is considered an acceptable time period for spray residues to dry.

6. **Comments on acreage limitations for potato crops.**
A comment was received in which it was suggested that an acreage limitation should not be applied to professional applicators who mix, load and apply acetamiprid to potato crops.

Response:

There was an error of omission presented in the mixer, loader, and applicator scenario (Table 6 of PRD2010-02) for the use of the closed-cab equipment by a farmer or professional applicator. The restriction of a maximum 19 kg of product per day also applies to an applicator wearing long-sleeved shirt, long pants, and no gloves while treating potato crops using closed-cab equipment. The mixing and loading was the greatest contributor to exposure. Using closed-cab application equipment did not afford significantly more protection (resulting in more hectares able to be treated) than using open-cab application equipment. Therefore, there was no reason to distinguish between the two in the label statement.

For the ASSAIL 70 WP Insecticide, the omitted row of Table 6 in Appendix I of PRD2010-02 for the closed-cab equipment is attached (see Table 1 of Appendix I).

References

A) Additional Information Considered

i) Published Information

Atkins EL, Kellum D, Atkins KW, 1981. Reducing pesticide hazards to honey bees: mortality prediction techniques and integrated management techniques. Univ Calif, Div Agric Sci, Leaflet 2883. 22 pp.

Hoenig, K., Hochrein, A., Quednow, B., Maier, B, Wagner, M. (2005) Impaired prepulse inhibition of acoustic startle in obsessive-compulsive disorder. Biological Psychiatry, 57(10): 1153-1158.

Takahashi H, Iwase M, Ishii R, Ohi K, Fukumoto M, Azechi M, Ikezawa K, Kurimoto R, Canuet L, Nakahachi T, Iike N, Tagami S, Morihara T, Okochi M, Tanaka T, Kazui H, Yoshida T, Tanimukai H, Yasuda Y, Kudo T, Hashimoto R, Takeda M. (2008). Impaired prepulse inhibition and habituation of acoustic startle response in Japanese patients with schizophrenia. Neuroscience Research, 62(3):187-94.

Table 1 Mixer/loader dermal and inhalation exposure estimates for Assail 70WP Insecticide - Addendum to Table 6 of PRD2010-02

Scenario			Mixer/Loader				Applicator				Total Body Exposure	
Farmers and Custom applicators, unless otherwise stated	Crop	Application rate (kg ai/ha)	Total Dermal unit exposure [a] (mg /kg ai handled)	Inhalation unit exposure [a] (mg /kg ai handled)	ATPD [b] (ha/day)	Body exposure [c] (mg ai/kg bw/day)	Applicator Scenario Equipment	Total Dermal unit exposure [a] (mg /kg ai handled)	Inhalation unit exposure [a] (mg/kg ai handled)	Body exposure [c] (mg ai/kg bw/day)	(inhalation + dermal) [d] (mg ai/kg bw/day)	MOE (target =300) [e]
M/L/A	Potato	0.0e02	0.1391	0.00502 (with respirator)	13.3/kg ai/d	7.53×10^{-3}	closed cab, groundboom, single layer, no gloves	0.01105	0.00006	2.219×10^{-4}	7.752×10	322

a. All M/L/A wear base personal protective equipment of single layer (long sleeved shirt and long pants) + chemical-resistant gloves, in addition, depending on scenario, M/L must wear chemical-resistant coveralls, and respirator

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number: 1117945
Reference: 2002, Dissociation Constant of IM-1-5, Data Numbering Code: 2.14.10

PMRA Document Number: 1117901
Reference: 2005, Assail 70 WP Insecticide, Two Year Storage Stability and Corrosion Characteristics, Data Numbering Code: 3.5.10

PMRA Document Number: 1526781
Reference: 2007, Acetamiprid 50 FS: Storage Stability and Corrosion Characteristics, Data Numbering Code: 3.5.10

PMRA Document Number: 1117798
Reference: 2005, Two Year Storage Stability and Corrosion Characteristics -10.3.2- An All Inclusive Report, Data Numbering Code: 3.5.10

2.0 Human and Animal Health

PMRA Document Number: 1117902
Reference: 2003, Determination of Acetamiprid Residues in Mature Lettuce Following Foliar Applications with Assail, BCS03-03, Data Numbering Code: 7.4.1

PMRA Document Number: 1117903
Reference: 2003, Determination of Acetamiprid Residues in Mature Celery Following Foliar Applications with Assail, BCS03-05, Data Numbering Code: 7.4.1

PMRA Document Number: 1117904
Reference: 2004, Acetamiprid: Magnitude of Residues in Broccoli and Cabbage Following Foliar Applications with Assail 70WP, NIS03103, Data Numbering Code: 7.2.1,7.4.1

PMRA Document Number: 1117905
Reference: 2004, Acetamiprid: Magnitude of Residues in grape Following Foliar Applications with Assail 70WP, NIS03102, Data Numbering Code: 7.2.1,7.4.1

PMRA Document Number: 1117906
Reference: 2004, Acetamiprid: Magnitude of Residues in Tomatoes Following Foliar Applications with Assail 70WP, NIS03101, Data Numbering Code: 7.2.1,7.4.1

PMRA Document Number: 1117907
Reference: 2003, Determination of Acetamiprid Residues in Mature Apples Following Foliar Applications with Assail, BCS03-02, Data Numbering Code: 7.4.1

PMRA Document Number: 1117908
Reference: 2003, Determination of Acetamiprid Residues in Mature Pears Following Foliar Applications with Assail, BCS03-04, Data Numbering Code: 7.4.1

PMRA Document Number: 1117909
Reference: 2005, NI-25 (Acetamiprid) Consideration of the Storage Stability in Confined Crop Rotational Study of Acetamiprid, Data Numbering Code: 7.4.3

PMRA Document Number: 1117941
Reference: 2002, Acetamiprid Waiver Request for Radiovalidation for IM-2-1 Amide, AC02-19, Data Numbering Code: 7.2.3

PMRA Document Number: 1449434
Reference: 2007, Percent Human Dermal Absorption for Acetamiprid, Data Numbering Code 4.3.8, 5.8

PMRA Document Number: 1453764
Reference: 2007, Acetamiprid Dermal Absorption Rate for Use in Occupational Risk Assessments, Data Numbering Code: 4.3.8

PMRA Document Number: 1117946
Reference: 2002, IM-1-5: Acute Oral Toxicity Study in Rats, H220, Data Numbering Code 4.2.1.

PMRA Document Number: 1117947
Reference: 2002, Acetamiprid Suspended in Corn Oil: Acute Oral Toxicity Study in Rats, H221, Data Numbering Code 4.2.1.

PMRA Document Number: 1117948
Reference: 2003, Metabolism Study of Acetamiprid in Rat (Determination of IM-1-5), NSM02-024, Data Numbering Code 4.5.9.

PMRA Document Number: 1117940
Reference: 2003, An Oral Developmental Neurotoxicity Study of Acetamiprid in Rats WIL-21193, Data Numbering Code 4.5.14.

PMRA Document Number: 1357277
Reference: 2006, Rebuttal of Data Evaluation Record for Acetamiprid, 21193, Data Numbering Code 4.5.14.

PMRA Document Number: 1449435
Reference: 2007, Acetamiprid DNT Study: NOAEL & LOAEL Evaluation (with explanatory notes added), EPA OPP HED Meeting, Data Numbering Code 4.5.14.

PMRA Document Number: 1453765
Reference: 2007, Characterization of Critical Toxicology Endpoints for Acetamiprid Risk Assessment: Auditory Startle Habituation and Maternal Toxicity from the Developmental Neurotoxicity Study, Data Numbering Code 4.5.14.

PMRA Document Number: 1449436
Reference: Non-GLP Statistical Analysis Conducted by Exponent, Inc. Acetamiprid DNT Study WIL-21193 MRID 46255619. Data Numbering Code 4.5.14.

PMRA Document Number: 1470632
Reference: 2007, Acetamiprid DNT Study (WIL-21193, MRID 46255619): Response to EPA CEB Statistical Analyses and Weight of Evidence Supporting NOAEL of 10 mg/kg bwt/day, Data Numbering Code 4.5.14.

3.0 Environment

PMRA Document Number: 1117942
Reference: 2003, Position statement on persistence and mobility of IM-1-5 in soil, Data Numbering Code 8.5.

PMRA Document Number: 1117944
Reference: 2003, 14C Acetamiprid: aged residue column leaching study in two calcareous soils, CX02018, RD-03103, Data Numbering Code 8.2.4.3.2.

PMRA Document Number: 1117943
Reference: 2002, 14C Acetamiprid: rate of degradation in three calcareous soils at 20°C, CX01013, RD-00168, Data Numbering Code 8.2.3.4.2.

PMRA Document Number: 1117945
Reference: 2002, Dissociation constant of IM-1-5, NCAS 02-132, Data Numbering Code 2.14.10.

PMRA Document Number: 1117957
Reference: 2003, Position paper on persistence of IM-1-4 in sediment, RD-03199, Data Numbering Code 8.5.

PMRA Document Number: 1117958
Reference: 2003, Position paper on IB-1-1, RD-03200, Data Numbering Code 8.5.

PMRA Document Number: 1117960
Reference: 1998, Evaluation of toxicity of residues of acetamiprid (NI-25) on alfalfa to honey bee (Apis mellifera), 98-1-7214, RD-03115, Data Numbering Code 9.2.4.

PMRA Document Number: 1117961
Reference: 2003, Acute contact and oral toxicity of EXP60707A to the bumblebee Bombus terrestris L. under laboratory conditions, 20021 073102-BLEU, Data Numbering Code 9.2.4

PMRA Document Number: 1117962
Reference: 2002, A semi-field study on the effects on honey bees (Apis mellifera L.) of ASSAIL 70 WP (EXP61842A, Acetamiprid 70%) Straight and in Combination with the Fungicide PROCURE 50WS (Triflumizole 50%), 20011239/SI-BZEU, Data Numbering Code 9.2.4

PMRA Document Number: 1117951
Reference: 2002, IM-1-5: acute toxicity to Daphnia magna, NCAS 01-197, RD-11 02414, Data Numbering Code 9.3.2

PMRA Document Number: 1117965
Reference: 2003, Acetamiprid Technical - Acute Toxicity to Midge (Chironomus riparius) Under Static Conditions, 12681 6104, Data Numbering Code 9.3.4

PMRA Document Number: 1117964
Reference: 2003, Acetamiprid Technical - Acute Toxicity to Gammarids (Gammarus fasciatus) Under Static Conditions, Data Numbering Code 9.3.4

PMRA Document Number: 1117969
Reference: 2003, Acetamiprid - Determination of Effects on Vegetative Vigour of Lettuce (Lactuca sativa), 02571-1075, 12681/6107, Data Numbering Code 9.8.4

PMRA Document Number: 1117967
Reference: 2000, Acetamiprid: A Reproduction Study with the Northern Bobwhite, 437-104, Data Numbering Code 9.6.3.1

PMRA Document Number: 1117968
Reference: 2004, Acetamiprid (NI-25) - Reproductive Toxicity Test with Mallard Duck (Anas platyrhynchos), 13798 4105, Data Numbering Code 9.6.3.2

4.0 Value

PMRA Document Number: 1117802
Reference: 2004, Control of European pine sawfly in Scotch pine with Tristar, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117803
Reference: 2005, Control of European pine sawfly in Scotch pine, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117916
Reference: 2005, Control of green peach aphid on tomato, Trial 1, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117917
Reference: 2005, Control of green peach aphid on tomato, Trial 2, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117918
Reference: 2005, Control of green apple aphid on red delicious apple, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117919
Reference: 2005, Control of green apple aphid on empire apple, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117920
Reference: Minimum effective rate of Assail against aphid pests of apple, Trial 1, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117921
Reference: Minimum effective rate of Assail against aphid pests of apple, Trial 2, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117922
Reference: 2003, Evaluation of Assail for control of aphids in lettuce, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117923
Reference: 2002, Evaluation of Assail for control of aphids in cauliflower, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117924
Reference: 2003, Evaluation of Assail for control of aphids in cauliflower, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117925
Reference: 2001, Control of first generation spotted tentiform leafminer, mullein leaf bug, and rosy apple aphid on apple, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117926
Reference: 2001, Control of first generation spotted tentiform leafminer and mullein leaf bug on apple with various insecticides, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117927
Reference: 2001, Assessment of insecticides for control of pear psylla and plum curculio on pear, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117928
Reference: 2002, Control of pear psylla on pear with insecticides, Data Numbering Code 10.2.3.3

B. Additional Information Considered

I) Published Information

1.0 Human and Animal Health

Ajarem, J.S. and Ahmad, M. (1998). Prenatal nicotine exposure modifies behavior of mice through early development. Pharmacology Biochemistry and Behavior, 59:313-318.

Banerjee, T.D., Middleton, F., Faraone, S.V. (2007). Environmental risk factors for attention-deficit hyperactivity disorder. Acta Paediatrica 96:1269-1274.

Dwyer, J.B., Broide, R.S, Leslie, F.M. (2008). Nicotine and brain development. Birth Defects Res. C. Embryo Today, 84:30-44.

Levin, E.D., Briggs, S.J., Christopher, N.C., Rose, J.E. (1993). Prenatal nicotine exposure and cognitive performance in rats. Neurotoxicology and Teratology, 15:251-260.

Liang, K., Pytress, B.S., Chen, Y., Leslie, F.M., Weinberger, N.M., Metherate, R. (2006). Neonatal nicotine exposure impairs nicotinic enhancement of central auditory processing and auditory learning in adult rats. Eur. J. Neurosci. 24:857-866.

Shacka, J.J., Fennell, O.B., Robinson, S.E. (1997). Prenatal nicotine sex-dependently alters agonist-induced locomotion and stereotypy. Neurotoxicology and Teratology, 19:167-176.

Slikker, W. Jr., Xu, Z. A., Levin, E.D., Slotkin, T.A. (2005). Mode of action: Disruption of brain cell replication, second messenger, and neurotransmitter systems during development leading to cognitive dysfunction – developmental neurotoxicity of nicotine. Critical Reviews in Toxicology, 35:703-711.

Slotkin, T.A. (1998). Fetal nicotine or cocaine exposure: which one is worse? J. Pharmacol. Exp. Ter. 285:931-945.

Thomas, J.D., Garrison, M.E., Slawecki, C.J., Ehlers, C.L., Riley, E.P. (2000). Nicotine exposure during the neonatal brain growth spurt produces hyperactivity in preweanling rats. Neurotoxicology and Teratology, 22:695-701.

Vaglenova, J., Birru, S., Pandiella, N.M., Breese, C.R. (2004). An assessment of the long-term developmental and behavioral teratogenicity of prenatal nicotine exposure. Behavioural Brain Research, 150: 159-170.

2.0 Environment

Iwasa T., Motoyama N., Ambrose J.T., Roe R.M. 2004. Mechanism for the differential toxicity of neonicotinoid insecticides in the honey bee, *Apis mellifera*. *Crop Protection* 23: 371–378.